REMARKS

This application is a divisional of U.S. Application Serial No. 08/996,422 and is directed to the compounds of formula I wherein m=1 and n=1 and pharmaceutical salts thereof, and pharmaceutical compositions containing such compounds. In the parent application restriction was required between the method of using the compounds and the compounds and pharmaceutical compositions. In addition election of a compound species was required. In the parent application Applicants elected the method of using a species falling within formula I wherein m=1 and n=1, reserving however the right to file divisional applications to all of the subject matter not examined in the parent application. The present amendment cancels all of the original claims and presents new Claims 91-145 directed to the pharmaceutical compositions and compounds of Applicants invention of formula IA/IB, a subgenus of formula I where m=1 and n=1.

The specification has been amended to provide the reference to the parent application and to correct typographical errors and avoid the use of the same substituent letter having different meanings. Thus where the letters Z and T have been given different meanings in defining a subgenus than given in the generic formula, Z and T have been changed to Z^a and T^a or T^b. Z has been redefined as Z′ in the claims, deleting the C(O) group from the definition of Z′ because the C(O) group now appears in the structural formula and omitting the case where T is -O- or -S- and X′ or X″ is hydroxy or fluoro. The specification has also been amended to provide antecedent basis for the cyclic formulas recited in original Claims 17, 19, 21 22, 24-27 and 30-31 (as well as corresponding composition and pharmaceutical composition claims). Table 7C (page 597) has also been amended to correct an error in the compound formula for 7C-214 in omitting the alaninyl moiety. Since this compound was prepared via a coupling reaction using an alaninyl-starting material, the product obviously must also contain an alaninyl-group. These amendments have also been made in the parent application. In addition the specification has been amended to provide antecedent basis for formula IA, recited in new Claim 91 representing the subgenus wherein

m=1 and n=1 and for formula IB in new Claim 93, wherein m=1 and n=1 but grouping the cyclic substituents (Q) recited in original pharmaceutical composition Claims 46-60 (as well as the corresponding compound claims).

New Claims 91-116 and 118-143, and 145 generally correspond to and are supported by the original pharmaceutical composition and compound claims defined for the case wherein m=1 and n=1. Support for the new pharmaceutical composition claim of formula IA, Claim 91, can be found in original Claims 32 and 33 wherein m=1 and n=1. Support for new Claim 92 can be found in original Claim 45. Support for the new pharmaceutical composition claim of formula IB, Claim 93, can be found in original Claims 46-60. In addition, the definition of R^2 in Claims 91 and 93 has been modified to provide antecedent support for the terms 2-aminopyridyl, 2-methylcyclopentyl, cyclohex-2-enyl and -$(CH_2)_4NHC(O)OC(CH_3)_3$ recited in Claim 116; see original Claim 44 and page 17, lines 8-30 of Applicants specification. In the substituent group -$(CH_2)_4$N-Boc, the term Boc has been replaced by *t*-butyloxycarbonyl (shown above) as defined for example on page 214 of the specification. Support for the inclusion of pharmaceutically acceptable salts can be found in the definition on page 160, lines 10-17 and original Claim 90. Claims 94-108 are ultimately dependent upon Claim 93 and support can be found in original Claims 45-60, respectively. Support for new Claims 109-114, more particularly defining the substituent group R^1, can be found in original Claims 36-42. In Claim 114, the formula $CH_3C(=NOH)CH_2$- and the formula for the 1,5-dimethyl-hex-4enyl correct obvious typographical errors found in original Claim 42 (page 778, line 18 and page 777, line 30, respectively). Further support for the first correction can be found in original Claim 90 and the compound 5-{N'-(4-(hydroxyimino)pentanoyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one. Support for Claims 115 and 116 more particularly defining the substituent group R^2 can be found in original Claims 43 and 44. Lastly, support for Claim 117 more particularly defining Z' as -CH_2- can be found in the definition of Z for example on page 10, lines 18-21 and the compounds recited on pages 18-86 of the specification, exemplifying the case where Z' is -CH_2-.

Parallel claims have also been presented to the compounds per se wherein m=1, n=1. Specifically, support for the new compound claims, Claims 118 and 120, can be found in original Claims 61 and 62 wherein m=1 and n=1 for formula I. Support for new Claim 119 can be found in original Claim 74. The definition of R^2 in Claims 118 and 120 has been modified in the same manner as discussed above with respect to Claims 91 and 93. As above noted, support for new Claim 120 can be found in original Claims 75-89. Support for the inclusion of pharmaceutically acceptable salts can be found in the definition on page 160, lines 10-17 and original Claim 90. Support for new Claims 121-135 can be found in original Claims 74-90. Support for new Claims 136-141, more particularly defining the substituent group R^1, can be found in original Claims 65-71. Claim 141 is supported as above with respect to Claim 114. Support for Claims 142 and 143 claims more particularly defining the substituent group R^2 can be found in original Claims 72 and 73, respectively. Claim 144 is supported in the same manner as discussed above with respect to Claim 115. Lastly, support for Claim 145 can be found in the specification on pages 18-88 and in original Claim 90.

In addition, unless otherwise expressly defined in the claims, the new claims now expressly recite that the terms aryl, aryloxy, alkaryl, heteroaryl and heterocyclic are optionally substituted to conform with the definitions of these terms in Applicants' specification; i.e. page 156, line 24 - page 157, line 9; page 157, lines 11-12; page 153, lines 27-29; page 158, lines 14-25 and page 158, line 27 - page 159, line 7, respectively.

Examination and allowance are respectfully requested.

In the event the Examiner has any questions concerning the Preliminary Amendment or the Application, the Examiner is requested to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,
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Date: July 26, 2001

Attachment A

Marked up version of the Specification

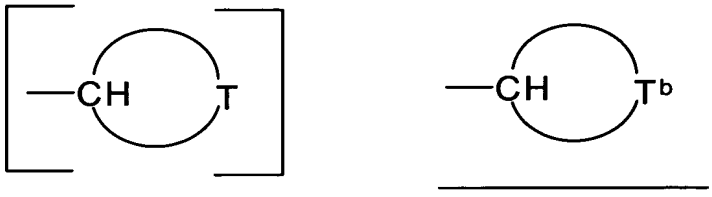
In accordance with the provisions of 35 U.S.C. §1.121(b)(iii), Applicants submit a marked up copy of the amendments made to the specification.

On page 1, paragraph 1, appearing under the section "Cross-Reference to Related Applications" please replace with the following paragraph:

This application [claims the benefit of] is a division of U.S. Application Serial No. 08/996,422 filed December 22, 1997, which claims priority under 35 U.S.C. §119(e) from U.S. Provisional Application No. 60/064,851 which was converted pursuant to 37 C.F.R. §1.53(b)(2)(ii) from U.S. Patent Application No. 08/780,025 filed December 23, 1996.

On page 87 paragraph 1, line 1-21 please replace with the following:

Preferred cyclic groups defined by W and $-C(H)_pC(=X)-$ include cycloalkyl, lactone, lactam, benzazepinone, dibenzazepinone and benzodiazepine groups. In one preferred embodiment, the cyclic group defined by W and $-C(H)_pC(=X)-$, forms a cycloalkyl group of the formula:



wherein [T] T^b is selected from the group consisting of alkylene and substituted alkylene.

On page 88, second full paragraph starting on line 8 through page 89, line 8 replace with:

In another preferred embodiment, the cyclic group defined by W, together with $-C(H)_pC(=X)-$ is a ring of the formula:

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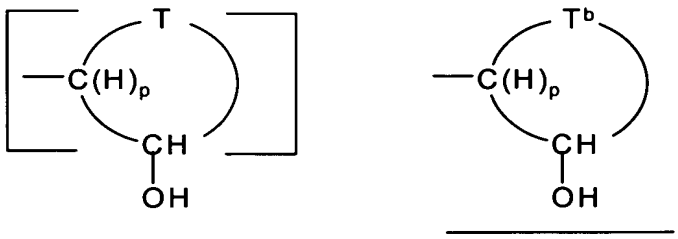
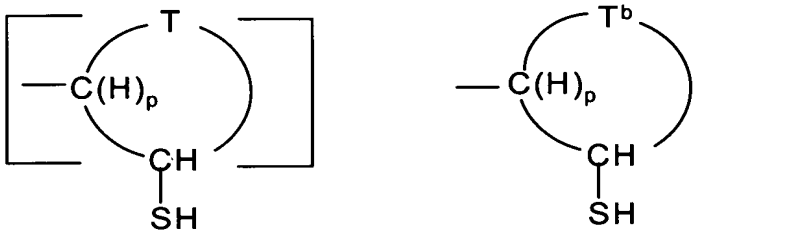


or



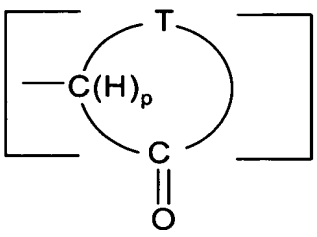
wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the
-O- or -S-, and *q* is an integer of from 1 to 3.

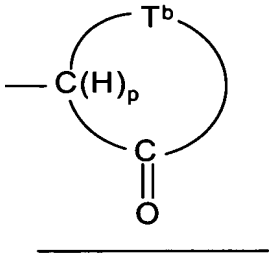
On page 90, second full paragraph starting at line 9 through page 91, line 10 replace with:

Yet another preferred embodiment of the cyclic group defined by W, together with

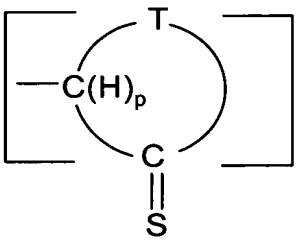
Attachment A

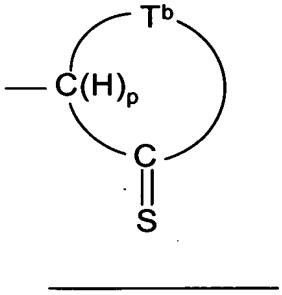
$-C(H)_pC(=X)-$, is a ring of the formula:





or





wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the

-O- or -S-, and *q* is an integer of from 1 to 3.

On page 92, second full paragraph starting at line 7 through page 93, line 37, replace with:

In another preferred embodiment, the cyclic group defined by W, together with

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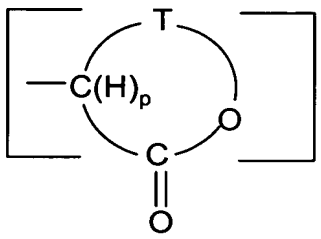
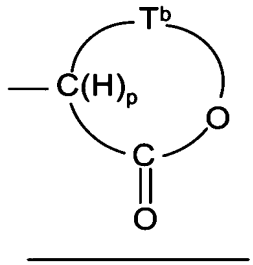
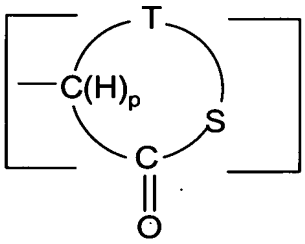
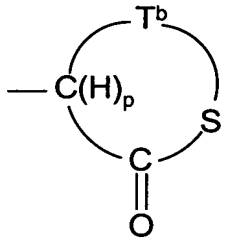
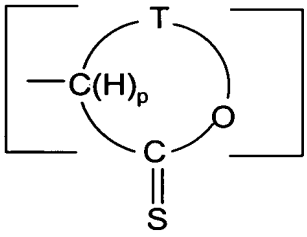
$-C(H)_pC(=X)-$, forms a ring of the formula:

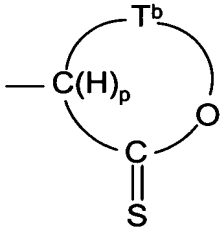






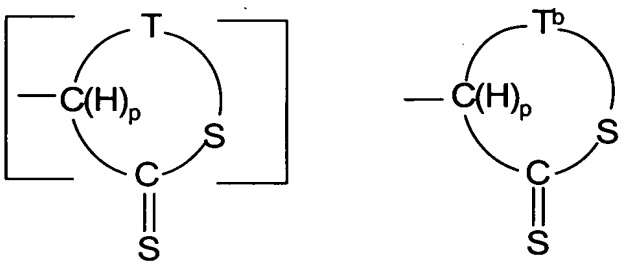






or

Attachment A



wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the
-O- or -S-, and *q* is an integer of from 1 to 3.

On page 94, second full paragraph, starting on line 20 through page 95, line 30, replace with:

In another preferred embodiment, the cyclic group defined by W and $-C(H)_pC(=X)-$, forms a lactam ring of the formula:

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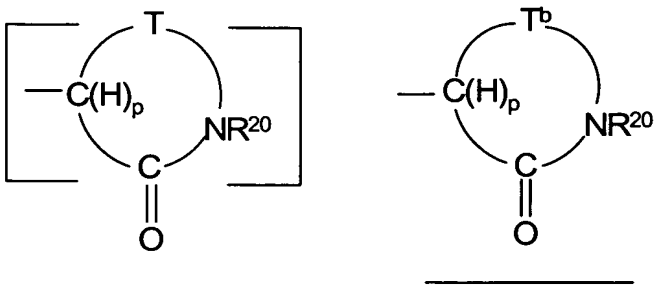
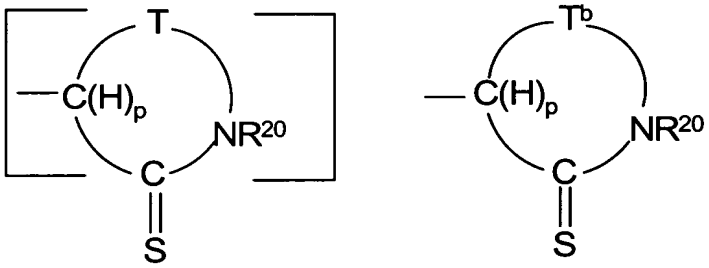


or a thiolactam ring of the formula:



wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the

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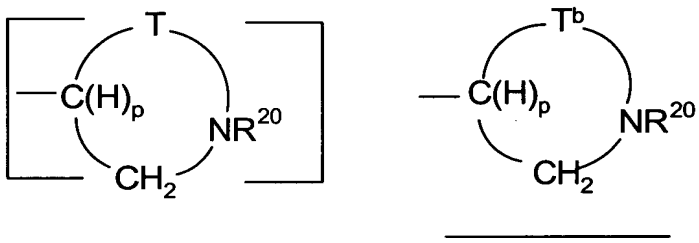
-O- or -S-, and *q* is an integer of from 1 to 3.

On page 99, first paragraph on lines 1-22, replace with:

In another preferred embodiment, the cyclic group defined by W, together with $-C(H)_pC(=X)-$, forms a ring of the formula:



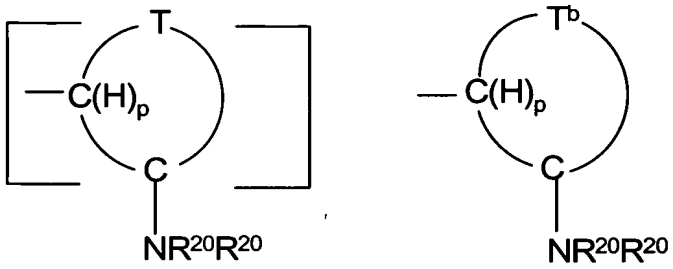
wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the

-O- or -S-, and *q* is an integer of from 1 to 3.

On page 99, second full paragraph starting at line 24 through page 100, line 10, replace with:

A still further preferred embodiment is directed to a ring group defined by W, together with $-C(H)_pC(=X)-$, of the formula:

Attachment A



wherein *p* is zero or one, [T] $\underline{T^b}$ is selected from the group consisting of alkylene, substituted alkylene, alkenylene, substituted alkenylene, [$-(R^{21}Z)_qR_{21}-$ and $-ZR^{21}-$ where Z] $\underline{-(R^{21}Z^a)_qR^{21}-}$ and $\underline{-Z^aR^{21}-}$ where $\underline{Z^a}$ is a substituent selected from the group consisting of -O-, -S- and $>NR^{20}$, each R^{20} is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, substituted alkyl, substituted alkenyl, substituted alkynyl, aryl, heteroaryl and heterocyclic, each R^{21} is independently alkylene, substituted alkylene, alkenylene and substituted alkenylene with the proviso that when [Z] $\underline{Z^a}$ is -O- or -S-, any unsaturation in the alkenylene and substituted alkenylene does not involve participation of the

-O- or -S-, and *q* is an integer of from 1 to 3.

Attachment A

Please replace page 597 of Table 7C with the section of the table below:

Example No.	Compound	Starting Material 1	Starting Material 2	General Procedure	MS
7C-214	5{N'-(dl-mandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	dl-mandelic acid or dl-alpha-hydroxyphenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2
7C-215	5-{N'-(p-chloromandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	p-chloromandelic acid (Acros)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	444.2, 478.1
7C-216	5-{N'-(1-alpha-hydroxyisocaproyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	1-alpha-hydroxyisocaproic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	424.2
7C-217	5-{N'-(4-bromomandelyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	4-bromomandelic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	522.1, 524.1
7C-218	5-{N'-(1-(+)-lactyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	1-(+)-lactic acid (Sigma)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	382.2, 454.2
7C-219	5-{N'-(d-3-phenylacetyl)-L-alaninyl}-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	d-3-phenylacetic acid (Aldrich)	5-(L-alaninyl)-amino-7-methyl-5,7-dihydro-6H-dibenz[b,d]azepin-6-one	C-P	458.2